

Remarks

I. Support for Amendments

Claims 1-17 have been amended to more clearly define the claimed invention. Support for these amended claims can be found throughout the Specification, for example on page 34 lines 10-16, page 35 line 28, page 35 lines 16-20 and Fig 2C row 4. Accordingly, no new matter is added by these amendments and entry therefore is respectfully requested.

II. Request for Reconsideration of Restriction Requirement Under 37 C.F.R. § 1.143

Election of Group I, claims 1-17, with traverse, has been entered by the Examiner and Group II, represented by claim 18, has been withdrawn without prejudice by the Applicants. Reconsideration is respectfully requested on the basis that search and examination of claim 18 can be made without undue burden (MPEP §803). In the event that the Examiner does not amend the requirement, Applicants respectfully request that the Examiner indicate that the requirement is made final.

III. Declaration for Patent Application Under 37 C.F.R. § 1.67(a)

As requested by the Examiner, a new corrected oath, providing the citizenship of Inventor Michela Visintin, is submitted herewith in compliance with 37 C.F.R. § 1.67(a).

IV. Request for Withdrawal of Office Action and/or Issuance of Supplemental Office Action Including Examiner's Consideration of References Cited in ISR Included in National Stage File

The Examiner states that the references cited in the International Search Report (ISR) have not been considered because it is asserted that a listing of the references cited in the ISR is not considered to be an IDS in compliance with 37 CFR 1.98. However, as indicated in an Office Communication dated November 1, 2001 (a copy of which is submitted herewith as Appendix A for the convenience of the Examiner) a copy of the ISR and copies of the references cited in the ISR are indicated to be present in the National Stage File. It is respectfully submitted that, in accordance with U.S. National Stage practice under 35 USC §371, the Examiner is to consider the documents cited in the International Search Report, without any further action by applicant under 37 CFR 1.97 and 1.98, when both the International Search Report and copies of

the documents are indicated to be present in the National Stage File and that the Examiner is to note the consideration in the first Office Action. MPEP § 1893.03(g).

Applicants respectfully point out that Gargano et al., cited by the Examiner in the instant Office Action, is among the references listed in the ISR, copies of which are part of the file. Accordingly, in the interests of completeness and clarity, Applicants respectfully request that the instant Office Action be withdrawn, and that a Supplementary Office Action be issued, in which the Examiner properly notes for the record the consideration of all the references cited in the ISR. MPEP § 707.07. Applicants further respectfully request that the time for response to the Supplementary Action be restarted to the extent additional response is required by the Applicants.

V. Objection of Claims 8-14 and 17 Under 37 C.F.R. § 1.75(c)

Claims 8-14 and 17 are objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim in reciting “A method according to any preceding claim.” Claims 2-17 have been amended to recite “The method of claim.” Accordingly, claim 1 as amended provides the proper antecedent basis for each of these dependent claims and withdrawal of this objection is respectfully requested. The Examiner is thanked for noting this informality in the claim language.

VI. Rejection of Claims 1-17 Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 1 to 17 under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1-17 have been amended to more clearly define the claimed invention. This ground of rejection is respectfully traversed. Applicants respectfully submit that claims 15 and 16, however, fully satisfy the requirements of § 112, second paragraph, as the person of ordinary skill would appreciate that the steps recited therein properly further limit the method of claim 1. As disclosed in the specification on page 4, lines 23-30, one embodiment of the invention comprises a functional assay for the immunoglobulin, which includes the further steps of selecting the immunoglobulins which cause a signal to be generated in the intracellular environment (step (e), claim 15), and subjecting those immunoglobulins to a functional intracellular assay (step (f), claim 16). The results of such a functional assay provide information on the binding ability of an immunoglobulin to a target in an intracellular

environment. Accordingly, withdrawal of the rejection is believed proper, and is respectfully requested.

VII. Rejection of Claims 1-17 Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1-17 under 35 U.S.C. § 102(b), as anticipated by Gargano et al. Gargano et al. is relied upon by the Examiner in this action for disclosing the determination of efficient binding between intracellular immunoglobulins expressed in a yeast two hybrid format and corresponding target antigens in an intracellular environment (yeast cells). The Examiner asserts that the assay disclosed in Gargano et al. provides a first molecule and a second molecule, a transcriptional activation domain and a DNA-binding domain, which exist as separate domains but associate to form an active reporter molecule. Activation of the reporter construct is asserted to occur when the two domains (VP16 and LexA) are brought together through the binding interaction of the two polypeptides fused thereto, a scFv fragment and a target antigen, respectively, leading to the generation of a signal that can be monitored by a colorimetric assay. The Examiner further asserts that Gargano et al. discloses that the level of reporter activation correlates well with specific binding of proteins, which further gives an indication of the strength of the interaction. This ground of rejection is respectfully traversed.

Accepting, *arguendo*, the Examiner's characterization of Gargano et al., the reference fails to anticipate the claims as amended. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Gargano et al. discloses a method wherein *one* intracellular antibody (Ab) is already known and gives a positive signal in an assay. Gargano et al. does not describe or suggest that their assay may be used to *select* intracellular Abs and/or *determine* the capacity of an Ab (whose intracellular behavior is not known) to bind intracellularly. In contrast, independent claim 1, as amended, recites a method for determining binding of an immunoglobulin to a target in an intracellular environment, comprising the steps of: a) providing, in an intracellular environment, a first molecule and a second molecule, wherein stable interaction of the first and second molecules leads to the generation of a signal, wherein an immunoglobulin is associated with the first molecule, and wherein an intracellular target is associated with the second molecule, such that binding of the immunoglobulin to the target leads to the specific interaction of the first and


second molecules and generation of the signal; and b) assessing the intracellular binding between the immunoglobulin and the target by monitoring the signal.

Thus, Gargano et al. does not teach every element of the claimed invention and therefore, does not anticipate amended claims 1-17. Accordingly, withdrawal of the rejection of claims 1-17 under 35 U.S.C. § 102(b) over Gargano et al. is respectfully requested.

VIII. Conclusion

In view of the foregoing remarks, Applicants believe that the application is in condition for allowance. However, if the Examiner disagrees, the Examiner is encouraged to call the undersigned at the number listed below in order to expedite the prosecution of this application.

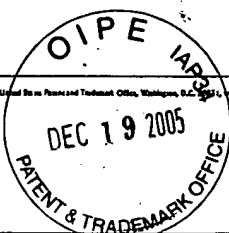
Respectfully submitted,

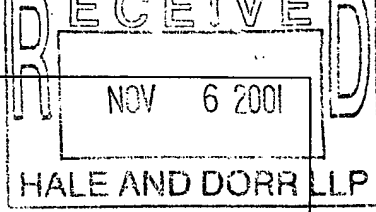


Henry N. Wixon
Attorney for Applicants
Registration No. 32,073

Date: 19 DECEMBER 2005
WILMER CUTLER PICKERING HALE AND DORR LLP
1455 Pennsylvania Ave., NW
Washington, DC 20004
Tel: (202) 942-8400
Fax: (202) 942-8484

Appendix A: Copy of Office Communication dated November 1, 2001





U.S. APPLICATION NUMBER NO. 09/936,170	FIRST NAMED APPLICANT Eric Tse	ATTY. DOCKET NO. 109312.120
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INTERNATIONAL APPLICATION NO. PCT/GB00/00876	
I.A. FILING DATE 03/10/2000	PRIORITY DATE 03/10/1999

Base Date: _____
 Call up Date: 11/16/01
 Due Date: 12/1/01 *Response to*
 Henry N Wixon Hale & Dorr
 1455 Pennsylvania Ave NW Suite 1000
 Washington, DC 20004 *Missing App.*
 Ext. _____ Dkt'd By W/d

CONFIRMATION NO. 9703

371 FORMALITIES LETTER



OC000000006991597

Date Mailed: 11/01/2001

DOCKETED BY SECRETARY _____

NOTIFICATION OF MISSING REQUIREMENTS UNDER 35 U.S.C. 371 IN THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as an Elected Office (37 CFR 1.495):

- U.S. Basic National Fees
- Priority Document
- Copy of IPE Report
- Copy of references cited in ISR
- Copy of the International Application
- Copy of the International Search Report

The following items **MUST** be furnished within the period set forth below in order to complete the requirements for acceptance under 35 U.S.C. 371:

- Oath or declaration of the inventors, in compliance with 37 CFR 1.497(a) and (b), identifying the application by the International application number and international filing date.

ALL OF THE ITEMS SET FORTH ABOVE MUST BE SUBMITTED WITHIN TWO (2) MONTH FROM THE DATE OF THIS NOTICE OR BY 22 or 32 MONTHS (where 37 CFR 1.495 applies) FROM THE PRIORITY DATE FOR THE APPLICATION, WHICHEVER IS LATER. FAILURE TO PROPERLY RESPOND WILL RESULT IN ABANDONMENT.

The time period set above may be extended by filing a petition and fee for extension of time under the provisions of 37 CFR 1.136(a).

Additionally the following defects have been observed:

- Additional claim fees of **\$36** as a non-small entity, including any required multiple dependent claim fee,

are required. Applicant must submit the additional claim fees or cancel the additional claims for which fees are due.

SUMMARY OF FEES DUE:

Total additional fees required for this application is **\$36** for a Large Entity:

- Total additional claim fee(s) for this application is **\$36**
 - **\$36** for 2 total claims over 20.

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

MAMIE P PERSON

Telephone: (703) 305-3737

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
09/936,170	PCT/GB00/00876	109312.